HIGHLIGHTS

HUMAN GENETICS

An unlikely association?

The first successful identification, by positional cloning, of genetic variants with an important function in a common human infectious disease has just been reported. The disease in question is leprosy, and Mira and Alcaïs *et al.* found that susceptibility to *Mycobacterium leprae* infection, the causative agent of the disease, is associated with polymorphisms in the upstream regulatory regions of the Parkinson disease gene *PARK2* and the co-regulated gene *PACRG*.

The authors previously mapped susceptibility to leprosy to a 6.4-Mb region on the short arm of chromosome 6. They used comparative sequencing and database searches to identify 64 SNPs in the region, such that at least one of them was associated with each of the 31 genes that reside in this region. Using these markers, they conducted an association scan among 197 Vietnamese families with two parents and one leprosy-affected child to find that the most significantly associated SNPs clustered in the regulatory region that is shared by *PARK2* and *PACRG*.

Comparative sequencing of the exons, 5′ and 3′ non-coding regions of both genes identified no coding SNP variants. Moreover, when the authors looked for more densely distributed markers in the regions of high association, all markers that were highly associated with susceptibility to leprosy clustered in that same 5′ regulatory region.

A look at the linkage-disequilibrium map of this 500-bp 5′ region showed that the variants that control susceptibility to leprosy lie in an 80-kb block. Multivariate statistical analysis showed that two SNPs in particular captured all of that association. Importantly, the authors subsequently confirmed these findings in an independent sample of almost 1,000 unrelated individuals from Rio de Janeiro, Brazil.

What might this unlikely association mean in biological terms? Although the function of *PACRG* is unknown, it has been implicated in the delivery of polyubiquitylated proteins to the proteasome, and *PARK2* itself encodes a ubiquitin E3 ligase. Both genes are expressed in immune tissues, in particular, to varying degrees, in Schwann cells and macrophages. Because both of these cell types are the primary host cells for *M. leprae*, these results highlight an exciting possibility that ubiquitin-mediated proteolysis might be important in the control of this infection, as well as neurodegeneration.

Magdalena Skipper

References and links

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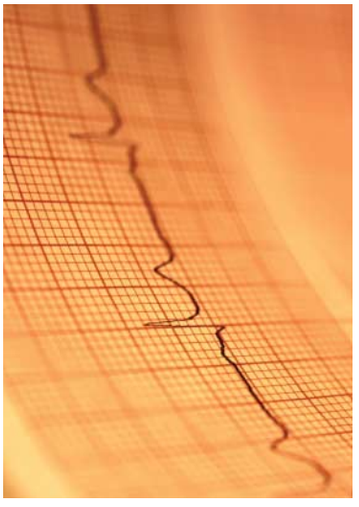
CANCER GENETICS

p53, a protein with a pulse



If there is one protein with little chance of leading a private life, it's p53. This tumour suppressor and its encoding gene have been thoroughly tinkered with over the years, with the result that we have a detailed molecular picture of how this so-called 'guardian of the genome' protects cells from genome damage by either promoting DNA repair or cell death. Galit Lahav and colleagues have now witnessed p53 at work in individual living cells. By fluorescently labelling human p53 and its regulator MDM2, they show that discrete p53 protein levels are activated in discrete quantities when DNA is damaged, and that the number of these 'pulses' depends on the severity of the damage.

The negative-feedback relationship between p53 and its partner MDM2 is well known: DNA damage lowers MDM2 levels, which in turn stabilize the p53 protein so that it can attempt to repair the damage. More p53 also means higher *MDM2* transcription and thereby p53 destabilization. To visualize these dynamics, the authors used time-lapse fluorescent microscopy on living human cells that expressed MDM2–YFP and p53–CFP fusion proteins, which glow yellow and cyan, respectively. The cells were zapped with gamma rays, which breaks DNA, and the levels of each protein were examined every 20 minutes for 16 hours. Fluorescence imaging is carried out routinely, but what is new here is the ability to look at individual cells, as the average signal that is released by a pool of cells would be impossible to resolve.

What the authors expected to see from this experiment was an 'analogue' behaviour, in which the strength of the output of the system matches the input — that is, where the amount of p53 protein increases in a graded manner with the severity of DNA damage. Instead, when the cells were irradiated, the two components of the p53–MDM2 feedback loop were activated in a series of discrete bursts, each containing a fixed amount of protein. The average height and duration of each pulse remained unchanged even when the DNA was more badly damaged; instead, the cells responded by increasing the number of pulses.

COMPARATIVE GENOMICS

Duplicating effort

Arguments have raged about how many times entire-genome duplications have occurred in vertebrate evolution (and indeed whether they have occurred at all!). "At least two" seems to be the answer based on the thorough comparative analysis of the human and *Fugu* genomes by Klaas Vandepoele, Wouter De Vos and their colleagues.

The sequencing of the *Fugu* genome was always going to be a key step in unravelling the twists and turns of vertebrate genome evolution. *Fugu* is a member of the sister group of land vertebrates, the ray-finned fish. In addition to the two genome duplications that are long-suspected to have occurred at the base of the vertebrate tree, some studies indicate that there has been another genome duplication in this group. However, preliminary analyses of the *Fugu* genome did not turn up evidence of an entire-genome duplication.

The authors realized that the most powerful way to address the question of vertebrate genome duplications was to do a comparative analysis. Using BLASTP, they searched for gene families that are shared by *Fugu* and human, and then added in homologous sequences from other fish, the mouse and the outgroups *Ciona* and *Drosophila*. They then built phylogenetic trees for each of the 3,077 gene families identified that had between two and ten *Fugu* genes.

The divergences between duplicated genes were dated relative to the ray-finned fish/land vertebrate divergence event within the 752 gene families in which there was strong statistical support for the relevant branches. The authors then estimated the absolute date of the divergences of gene duplicates in the 488 gene families and found evidence that a molecular clock was operating. A total of 166 (30%) of these divergences seem to have occurred between 225 and 425 million years ago (mya) — that is, after the ray-finned fish/land vertebrate split. Further analyses clearly indicated that a suite of duplicate genes arose approximately 320 mya. The implication is clear: an entire genome duplication event in an ancestor of ray-finned fish probably gave rise to many paralogues in the present-day *Fugu* genome.

However, the distribution of divergence times of *Fugu* gene paralogues is bimodal, with approximately 70% falling in the 500–900 mya window. So, it seems that there was probably at least one, and possibly two (roughly contemporaneous), genome-duplication events much earlier in vertebrate evolution — pre-dating the ray-finned fish/land vertebrate split and even the jawed/jawless vertebrate split (~575 mya). These data indicate that genome duplication has almost certainly had a large role in the evolution of all vertebrates.

These few ancient duplications of vertebrate genomes are fascinating; however, it will take a much more intensive sampling of vertebrate lineages before we will be able to effectively identify and analyse enough similar duplications to start making some generalizations about these events and their consequences.

Nick Campbell

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WEB SITE

Yves Van de Peer's Laboratory: http://www.psb.ugent.be/bioinformatics

This behaviour — which is described as 'digital' because the magnitude of the input is translated into a number of discrete outputs — is important in some biological systems, such as spiking neurons, but defies theoretical expectations of how a negative-feedback relationship should operate. It's a trickly problem to address, but the authors speculate that the gradual increase in p53 protein that is afforded by repeated pulses is a fail-safe mechanism that prevents the downstream repair enzymes from swamping the cell and triggering its death.

Tanita Casci

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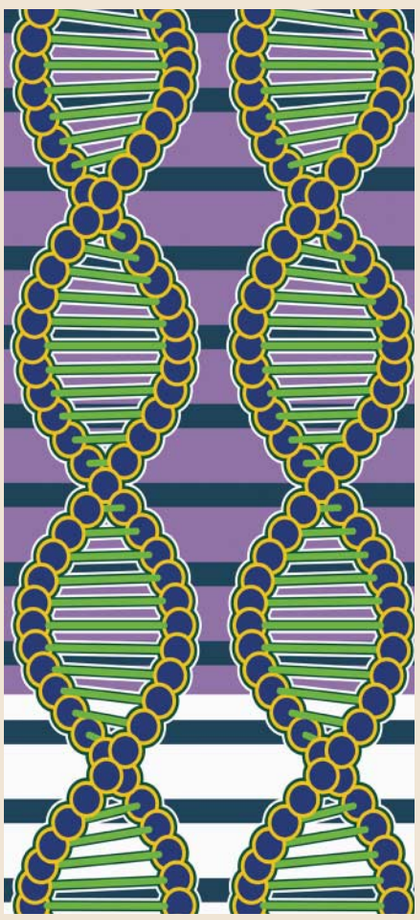
WEB SITE

Uri Alon's laboratory: http://www.weizmann.ac.il/mcb/UriAlon



DEVELOPMENTAL BIOLOGY

Those tricky first steps

Every parent anxiously awaits their little one's first word or wobbly steps, but the most significant developmental milestone happened much earlier, when the oocyte became an embryo and established itself in the lining of the womb. This early stage in a mammal's life is tucked away and so cannot be studied genetically using phenotypic assays. Two groups have now investigated the development of the mouse pre-implantation embryo using microarray-based transcriptional profiling. They show that it is possible to build a temporal profile of gene expression on which to base hypotheses about how genes interact during this early stage of life.

Q. Tian Wang and colleagues examined the expression profile of ~12,000 genes across 12 morphological time points from unfertilized egg to late blastocyst. The expression of a surprising number — more than one-third — of the genes varied by more than fivefold during this period. As well as being sensitive in identifying genes for which transcripts go up or down, the method also faithfully picked up the complexity of a particular stage, such as the increased transcript complexity that occurs following fertilization owing to the transition from maternal gene expression to zygotic genome activation (ZGA). Perhaps the most revealing discovery was that several members of familiar signalling pathways, such as those downstream of Notch, Wnt and BMP, were active at several crucial times — just before implantation, for example — thereby providing candidate genes for further study. The temporal resolution afforded by the array also allows promising candidates to be selected by virtue of their co-expression with known genes.

A similar analysis — this time by monitoring the expression of ~22,000 genes over 7 defined morphological pre-implantation stages — was carried out by Toshio Hamatami and colleagues. A general look at global-transcription trends defines two main developmental transitions — one at the 0–2-cell stage, when ZGA begins, and another, unanticipated one, at the 4–8-cell transition. A thorough study of the behaviour of individual genes that were expressed at each stage revealed some new and useful information: most gene transcription is activated in four transient waves that quickly tail off. This peculiar pattern indicates that many genes are stage-specific (a conclusion also drawn by Wang *et al.*); short bursts of expression presumably ensure that one stage-specific gene product does not spill over into the next stage. But how might these transitions be timed? Experiments *in vitro* that use gene-expression inhibitors support the view that the first wave, which coincides with ZGA, might be activated by maternal factors, with the following waves depending on genes that were expressed in the immediately preceding one, in a stepwise fashion.

The two reports do not always agree: for example, Wang *et al.* found that the main developmental transition occurs at the 2–4-cell stage. Nevertheless, this is the first time that microarrays have been applied to the study of pre-implantation development in the mouse and they have produced a thorough, accurate and quantitative picture of early embryonic development. What's more, they have provided us with a list of genes — thousands of them — to follow up on.

Tanita Casci

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ORIGINAL RESEARCH PAPERS Hamatani, T. *et al*. Dynamics of global gene expression changes during mouse preimplantation development. *Dev. Cell* **6**, 117–131 (2004) | Wang, Q. T. *et al*. A genome-wide study of gene activity reveals developmental signaling pathways in the preimplantation mouse embryo. *Dev. Cell* **6**, 131–144 (2004)

IN THE NEWS

Peer review — the big secret?

Three quarters of the British public have no idea what peer review is, according to a new poll that was commissioned by the Science Media Centre and *Nature*.

The poll, conducted by the MORI Social Research Institute, involved interviewing more than a 1,000 adults aged 15 and over. The results were startling or unsurprising, depending on your point of view — only a quarter of those interviewed described peer review as "society's scrutiny of other scientists' work, generally" (BBC Radio 4, Today programme). Intriguingly, however, the survey also showed that the public supports rigorous scrutiny of scientific results before publication, and if peer review did not exist already they would want to create it. "The vast majority (71%) of the public favour either the kind of scrutiny provided by peer review or more stringent controls in which experiments are repeated independently before being published" (*The Guardian*). Fiona Fox, director of the Science Media Centre, encouraged the scientists to "get out there and share their big secret" of peer review.

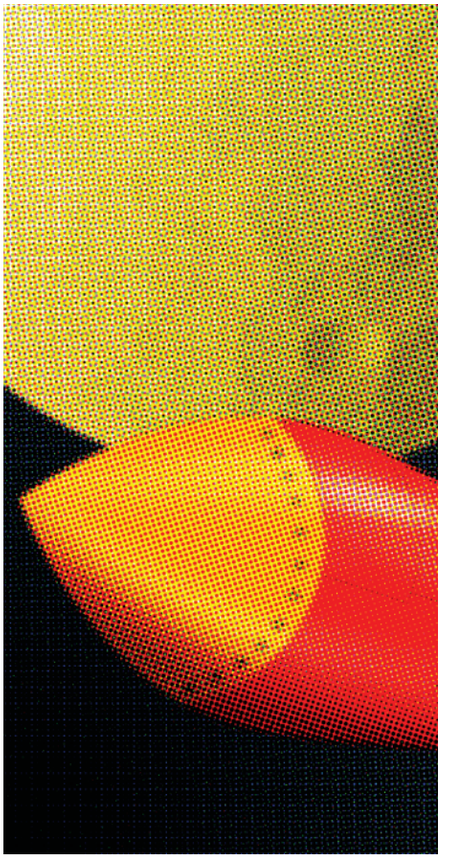
These findings are of course timely — they were published only a few days after the "IVF specialist Dr Panos Zavos announced to the press that he had cloned a baby" having "refused to submit his experiment to peer review" (*The Guardian*). So, the poll's results seem to say that it is not only the scientists who are frustrated with this kind of science reporting, but that the public is weary as well.

There is a constructive outcome to this survey — the Science Media Centre has published a new guide for scientists "in an effort to help them better communicate their work" (*The Guardian*).

Magdalena Skipper

GENOME EVOLUTION

Escape from Planet X



Genes on the mammalian X chromosome just can't wait to get off.

J. J. Emerson and colleagues' analysis of the human and mouse genomes shows that the X chromosome has a clear excess of genes that have functional duplicates on other chromosomes. Of the 94 genes that the authors identified to have been functionally retroposed between chromosomes in the human genome, 15 were derived from X-chromosome genes: far more than the 3 or 4 expected on the basis of the size of this chromosome. Similarly, the 17 out of 105 functional retropositions in the mouse genome were of X-chromosome genes, although only 4 or 5 were expected.

So why do genes want out of the X chromosome? One possibility is that genes that benefit males at a cost to females are moving because, compared with the X chromosome, an autosome spends on average less time in females and so would be more difficult to select against. Alternatively, the inactivation of X-linked genes during meiosis might favour the export of genes to the autosomes, where they are more likely to be expressed to the benefit of the male during meiosis. Either of these mechanisms could cause functional retrogenes that are exported from the X to be selectively favoured over genes that are retroposed from other chromosomes.

Despite the X chromosome being a popular place for genes to leave, paradoxically, it also seems that it is a favourite destination. The authors show that there are relatively many more functional retrogenes recruited to the X than any other chromosome in both human and mouse genomes. However, they also show that human pseudoretrogenes, which are less likely to be subject to selection, are also more common than expected on the X chromosome. So, although selection once again has a key role in causing this bias, in this case there is likely to be a purely mechanistic component to the bias.

So, it seems that selection primarily powers the genic traffic that

TECHNOLOGY

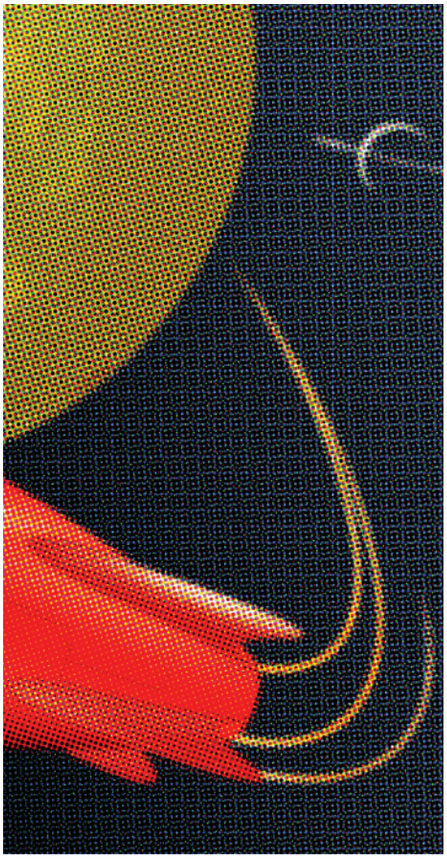
A robot scientist

Thanks to a new system developed by Ross King *et al.*, scientists could soon be spending less time formulating and testing hypotheses and more time making "…the high-level creative leaps at which they excel".

King *et al.* have developed a 'robot scientist' that takes the integration of robotics and scientific discovery to a new level. It consists of a master computer that controls the system and carries out the scientific reasoning, a liquid-handling robot and a plate reader, along with their control computers. It runs software that includes background biological information, a logical inference engine and codes that generate hypotheses, select experiments and integrate the whole system.

Functional genomics was the testing ground for the robot scientist: specifically, dissection of the yeast aromatic amino acid (AAA)-synthesis pathway. First, the authors developed a 'logical formalism', which translates biological data into formulae for the computer. For the AAA pathway, data were taken from the *Kyoto Encyclopedia of Genes and Genomes* (KEGG). Using the logical formulae, Prolog, the robot scientist's logic-programming language, then generated a model of the AAA pathway. Next, the robot scientist formulated hypotheses about the relationships between AAA-enzymatic reactions and open reading frames, devised and ran experiments to test them, interpreted the results to discount inconsistent hypotheses, and so on. The robot scientist essentially performed as well as human scientists, predicting at least 80% of all possible experiments.

Next, King *et al.* compared the accuracy (that is, the number of correct predictions made) versus the monetary cost of different experimental selection strategies. In the long term, the robot scientist's machine-learning system — active selection of experiments (ASE)-Progol — was more cost effective than choosing the cheapest experiment or a random experiment.



travels to and from the mammalian X chromosome. However, is the cement still wet on this busy genomic highway or is it a well-worn track? Emerson and colleagues answer this question with a comparative analysis of the mouse and human genomes, which showed that most retrogenes that have escaped the X (12/15) or have moved to it (10/13) did so before the mouse–human divergence. Clearly, the turnover of genes on the X chromosome is an ancient but ongoing process.

The fascinating picture of dynamic X-chromsome evolution that Emerson and colleagues have revealed invites a bit of genomic crystal-ball gazing. Is it just a matter of time before the X chromosome becomes the exclusive preserve of genes that are advantageous to males when hemizygous and that are silenced in female tissues, whereas all genes that are favourable to males when homozygous will be shifted to the autosomes?

Nick Campbell

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WEB SITES
Esther Betran's laboratory: http://www3.uta.edu/faculty/betran
Henrik Kaessmann's laboratory: http://www.unil.ch/cig/page6396_en.html
Manyuan Long's laboratory: http://pondside.uchicago.edu/~longlab/longlab.html

However, before robot scientists appear in laboratories everywhere, there is still a lot of work to be done. The authors are now testing whether their system can uncover the role of genes for which no functional information is available. This will require the translation of many bioinformatic databases into logical formulae and the extension of their hypothesis-generation method. But it does seem that the potential of this system to be applied to many scientific problems will ensure that, one day, the use of robot scientists will be commonplace.

Natalie Wilson

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WEB SITES
ASE-Progol: ftp://www.comp.rgu.ac.uk/pub/staff/chb/systems/ase_progol/version_1.0
KEGG: http://www.genome.ad.jp/kegg

IN BRIEF

DEVELOPMENTAL BIOLOGY

fgf8 mRNA decay establishes a gradient that couples axial elongation to patterning in the vertebrate embryo.

Dubrulle, J. & Pourquié, O. *Nature* **427**, 419–422 (2004)

Axial development in vertebrate embryos proceeds in a stereotypical manner whereby cells differentiate according to their position in a protein gradient. This paper shows how the Fgf8 gradient that controls this process might form in the chick. *fgf8* is transcribed only in tail-bud cells but this process stops as these cells move anteriorly during development. The protein gradient is consequently formed as the cells' supply of mRNA dwindles, therefore providing the answer to a long-standing question.

POPULATION GENETICS

Evidence for extensive transmission distortion in the human genome.

Zöllner, S. *et al. Am. J. Hum. Genet.* **74**, 62–72 (2004)

Mendel's laws predict that a diploid organism should transmit each chromosome at a similar frequency. Deviations from this 1:1 ratio — known as segregation distortion — occur in many species and for various reasons. By examining genome data from 148 families, the authors conclude that segregation distortion is extensive in humans and that many loci underlie this effect.

GENE REGULATION

A noncoding RNA is required for the repression of RNApol II-dependent transcription in primordial germ cells.

Martinho, R. G. *et al*. *Curr. Biol*. **14**, 159–165 (2004)

Unlike somatic cells, primordial germ cells (PGCs) — those that will develop into eggs and sperm — need to remain undifferentiated: they are thought to do so by inhibiting RNApolII transcription. Ruth Lehmann's group has now found that a non-coding RNA that is encoded by the *polar granule component* (*pgc*) gene blocks RNApolII activity in PGCs, possibly by preventing transcription-activating enzymes from reaching the nucleus.

MEDICAL GENETICS

Molecular and comparative genetics of mental retardation.

Inlow, J. K. & Restifo, L. L. *Genetics* (in the press)

Mental retardation (MR) is a common and genetically heterogeneous form of cognitive impairment. Jennifer Inlow and Linda Restifo estimate there to be hundreds of MR genes, 282 of which they have identified by data mining the Online Mendelian Inheritence in Man (OMIM) database and the literature. A total of 76% of these genes have functional orthologues in *Drosophila*, which indicates that this fly could be the ideal model to use to dissect the genetic basis of MR.

WEB WATCH

SARS resource

• http://www.ncbi.nlm.nih.gov/genomes/SARS/SARS.html

With the recent confirmation of a new outbreak of severe acute respiratory syndrome (SARS), the possibility that this disease will become a major killer is a real concern. Modern diagnostic tests, antiviral agents and vaccines are all needed to combat the disease, and these require sequence data and the functional dissection of the genome of the SARS coronavirus.

To this aim, in May 2003, the National Center for Biotechnology Information (NCBI) set up the SARS coronavirus resource to provide "…the most recent sequences, annotations, and analysis…". And with the most recent update in February 2004, to include data from the Chinese SARS Molecular Epidemiology Consortium, this really does seem to be the case.

On the web site, there is the option to view pre-computed global alignments of the genomes of various isolates. The complete sequence data of both genes and proteins are also available, along with their pre-computed analysis. Of course, with the availability of the BLAST alignment tool, there is also the option to carry out your own analysis.

Combine all of this with links to the most recent SARS publications and other useful SARS-related information — from organizations such as the Center for Disease Control and Prevention (CDC), the World Health Organization (WHO) and Medline Plus — and this really is a web site that is worth bookmarking by those who want to keep up to date with the field.

Natalie Wilson

FURTHER READING The Chinese SARS Molecular Epidemiology Consortium. Molecular evolution of the SARS coronavirus during the course of the SARS epidemic in China. *Science* 29 Jan 2004 (doi:10.1126/science.1092002)

HUMAN GENETICS

Perfect match

Some very simple strategies for matching cases and controls can deal with the persisent bugbear of association studies — structured populations.

In structured populations, subgroups can differ in both their susceptibility to a disease and a suite of other unrelated characters. If disease cases and controls are selected at random, the more-susceptible population subgroup will be more common in cases than it is in the population as a whole, whereas the less-susceptible subgroup will be similarly over-represented in the controls. The trouble is that when the cases and controls differ in their composition with respect to these population subgroups, the genes underlying the unrelated characters that differ between subgroups can be spuriously associated with the disease. Now, David Hinds and colleagues show that several simple matching strategies can eliminate stratification from population samples.

The Mexican population that they studied is a classic case of admixture: indigenous Indians and Caucasians of Spanish European ancestry have both made substantial contributions to the present-day populace, most of whom regard themselves as 'Mestizo' — mixed ancestry. As Caucasians tend to be taller than Indians, the authors expected that any unmatched association study of height — the model complex trait — would be confounded with ancestry.

This intuitive assessment of the system proved to be spot on: many of the 275 SNPs typed from the genome of 707 individuals differed in allele frequencies among the self-assessed ancestral categories. Moreover, a genotype-based analysis of population structure in the sample defined two distinct subpopulation clusters — A and B — which correspond to groups with largely European or Indian ancestry, respectively. These clusters hopelessly confounded the predefined 'case' and 'control' groups of tall and short individuals: many SNPs were spuriously associated with height merely because of the differences in ancestry between these groups.

So, in a system that is so plagued by confounding population stratification, could a simple matching scheme remove the possibility of spurious associations?

The authors tried two matching strategies: in one, they removed individuals from the tall and short groups with the largest proportions of confounding ancestry until the average proportions in these groups were equal, whereas in the other, individuals were reselected for the tall and short groups after adjusting the value of their height to take into account differences in ancestry. Both strategies largely removed the telltale signs of population stratification in the data.

Simple matching strategies such as these, based on a limited set of genotyped SNPs, could eventually be the standard prelude to a large-scale genotyping effort on pooled DNA. Such an approach would seem to provide the best of both worlds: the confidence that the whole-genome association study has been controlled for population stratification without the need for genotyping millions of SNPs individually.

Nick Campbell

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WEB SITE

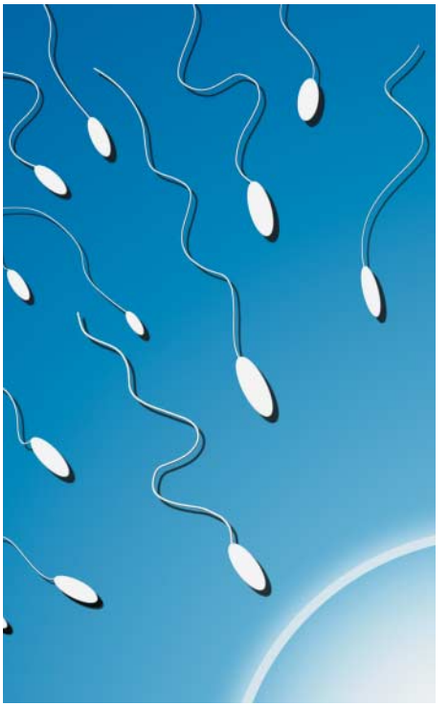
Perlegen Sciences: http://www.perlegen.com

TECHNOLOGY

Fish sperm made to order

Mice are the envy of the genetics world thanks to the ease with which these animals can be genetically altered by tinkering with cultured embryonic stem (ES) cells. When it comes to making straight transgenics, however, the mouse no longer stands apart: for this and most other species, DNA needs to be injected into embryos or germ cells, which leads to a low but nevertheless unwelcome degree of mosaicism. Kayoko Kurita and colleagues have discovered how to do away with such inefficiencies: they have successfully created transgenic sperm by genetically modifying zebrafish sperm precursors that are grown *in vitro*.

Hundreds of developmental zebrafish mutants have been created, and the genome sequencing project has highlighted many more genes that could be modified or inactivated. The available options for fish transgenesis, however, are currently inadequate: for example, when DNA is injected into oocytes, embryos or the male pronucleus of a zygote, the resulting transgenic organism is usually mosaic for the transgene, meaning that germline transmission cannot be ensured until the following generation. The most straightforward way of avoiding this inconvenience would be to genetically modify sperm before fertilization, so that all cells of the F_1 progeny contain the transgene; however, this approach has not been met with much success, *in vivo* or *in vitro*, as mature sperm are refractory to transgene insertion.



To avoid the problem, Kurita and co-workers set out to introduce the transgene into sperm precursors. Primary cultures of zebrafish male germ cells were infected with retroviral vectors derived from the Moloney murine leukaemia virus. The *in vitro* matured sperm were then used to produce transgenic offspring. Of the 89 successfully fertilized eggs that developed into adult fish (out of 104), 5 carried the transgene. Importantly, the transgene was transmitted to offspring in a Mendelian fashion, thereby proving that the parent fish was not mosaic.

Five transgenic fish out of 89 might not seem like a vastly high rate of insertion. However, this is comparable to the rate of success of current transgenic approaches, which lead to mosaic progeny. The authors speculate that their protocol — with the appropriate tweaks — could be applied to rapidly alter the sperm genomes of other animals, including humans.

Tanita Casci

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ETHICS WATCH

The threatened trade in human ova

It is well known that there is a shortage of human ova for *in vitro* fertilization (IVF) purposes, but little attention has been paid to the way in which the demand for ova in stem-cell technologies is likely to exacerbate that shortfall and create a trade in human eggs. Because the 'Dolly' technology relies on enucleated ova in large quantities, allowing for considerable wastage, there is a serious threat that commercial and research demands for human eggs will grow exponentially from the combination of these two pressures. In the absence of legal regulation in the United Kingdom, and in the context of a globalized trade in human organs, we face a 'Wild West' situation in genetic and biotechnological research that involves human ova.

A recent example shows how ineffective the Human Fertilisation and Embryology Act 1990 is likely to be in regulating or stopping this trade. In a research trial, Leeds General Hospital has admitted to paying women £1,500 to undergo an IVF cycle to harvest their eggs. Commentators in the UK might have thought we would be protected from the excesses that are prevalent in the United States, where there are documented cases of extraction for profit of up to 70 ova from a single cycle in one woman (who nearly died in the process)[1]. It turns out, however, that if eggs are never fertilized, the Human Fertilisation and Embryology Authority is powerless to intervene. In the Leeds case, the eggs were used by a pharmaceutical company for trials of improved techniques for *in vitro* maturation, during which eggs are ripened in the laboratory instead of in the ovaries. They were never fertilized. This would also be true of eggs used in stem-cell technologies.

So we face a future situation in which women in the United Kingdom are offered whatever the Local Research Ethics Committee (LREC) will condone and the 'market' will bear. That market is also likely to become globalized: already there are indications that eastern European women's ova are being extracted and sold illicitly by health-care professionals — a recent Croatian case involving two gynaecologists being a recent example. Elsewhere in eastern Europe — particularly in Russia, Bulgaria, Romania, Georgia and the Ukraine — a well-organized network that trades more generally in human organs has already been documented[2].

In the Leeds case, the LREC rejected an original offer by the drug company of £4,000 per woman , on the grounds that this would constitute a financial inducement rather than recompense for subjects' "time and hardship". By the drug company's standards, the United Kingdom would represent a cheap market even at that price, as the going rate in the United States is US $30,000–$40,000 for one cycle's eggs. The eggs of women from eastern Europe or developing countries would presumably be even cheaper[3]. Unless legislation action is taken quickly to close the loophole in the Human Fertilisation and Embryology Act — that leaves unregulated the trade in eggs that are not intended to be fertilized — we face the risk of a 'free-for-all' that will imperil both women's health and the future of stem-cell research.

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